

6403770

Neutrokin- α

1 AAATTCAGGATAACTCTCCTGAGGGGTGAGCCAAGCCCTGCCATGTAGTGCACGCAGGAC 60

61 ATCAACAAACACAGATAACAGGAAATGATCCATTCCCTGTGGTCACTTATTCTAAAGGCC 120

121 CCAACCTTCAAAGTTCAAGTAGTGATATGGATGACTCCACAGAAAGGGAGCAGTCACGCC 180
1 M D D S T E R E Q S R L 12

181 TTA CTTC TTGCCTTAAGAAAAGAGAAGAAATGAACTGAAGGAGTGTGTTTCCATCCTCC 240
13 T S C L K K R E E M K L K E C V S I L P 32
CD-I

241 CACGGAAGGAAAGCCCCTCTGTCCGATCCTCCAAAGACGGAAAGCTGCTGGCTGCAACCT 300
33 R K E S P S V R S S K D G K L L A A T L 52
CD-I

301 TGCTGCTGGCACTGCTGTCTTGCTGCCTCACGGTGGTGTCTTTCTACCAGGTGGCCGCC 360
53 L L A L L S C C L T V V S F Y Q V A A L 72

361 TGCAAGGGGACCTGGCCAGCCTCCGGGCAGAGCTGCAGGGCCACCACGCGGAGAAGCTGC 420
73 Q G D L A S L R A E L Q G H H A E K L P 92
CD-II

421 CAGCAGGAGCAGGAGCCCCAAGGCCGGCCTGGAGGAAGCTCCAGCTGTACCGCGGGAC 480
93 A G A G A P K A G L E E A P A V T A G L 112
CD-III

481 TGAAAATCTTTGAACCACCAGCTCCAGGAGAAGGCAACTCCAGTCAGAACAGCAGAAATA 540
113 K I F E P P A P G E G N S S Q N S R N K 132
#

541 AGCGTGCCGTTCAAGGTCCAGAAGAAACAGTCACTCAAGACTGCTTGCAACTGATTGCAG 600
133 R A V Q G P E E T V T Q D C L Q L I A D 152
CD-IV

FIG.1A

Neutrokin- α

```

601 ACAGTGAAACACCAACTATACAAAAAGGATCTTACACATTGTTCATGGCTTCTCAGCT 660
153 S E T P T I Q K G S Y T F V P W L L S F 172
                                CD-V

661 TTAAAAGGGGAAGTGCCCTAGAAGAAAAAGAGAATAAAATATTGGTCAAAGAACTGGTT 720
173 K R G S A L E E K E N K I L V K E T G Y 192
      CD-V                                CD-VI

721 ACTTTTTTATATATGGTCAGGTTTTATATACTGATAAGACCTACGCCATGGGACATCTAA 780
193 F F I Y G Q V L Y T D K T Y A M G H L I 212
      CD-VI                                CD-VII

781 TTCAGAGGAAGAAGGTCCATGTCTTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGAT 840
213 Q R K K V H V F G D E L S L V T L F R C 232
      CD-VII                                CD-VIII

#
841 GTATTCAAATATGCCTGAAACACTACCCAATAATTCCTGCTATTTCAGCTGGCATTGCAA 900
233 I Q N M P E T L P N N S C Y S A G I A K 252
      CD-VIII                                CD-IX

901 AACTGGAAGAAGGAGATGAACTCCAACCTTGCAATACCAAGAGAAAATGCACAAATATCAC 960
253 L E E G D E L Q L A I P R E N A Q I S L 272
      CD-X

961 TGGATGGAGATGTCACATTTTTTGGTGCATTGAACTGCTGTGACCTACTTACACCATGT 1020
273 D G D V T F F G A L K L L 285
      CD-XI

1021 CTGTAGCTATTTTCCTCCCTTTCTCTGTACCTCTAAGAAGAAAGAATCTAACTGAAAATA 1080

1081 CCAAAAAAAAAAAAAAAAAAAAAA 1100

```

FIG.1B

	10	20	30	
1	MSTESMIR	DEL	- - - - -	TNFalpha
1	M - - - -	- - - - -	- - - - -	TNFbeta
1	MGA - - -	- - - - -	- - - - -	LTbeta
1	MQQPFNYP	QIYW -	VDSSASSPW	FasLigand
1	MDDSTEREQ	SRL	TSCCLKREEMKL	Neutrokine alpha
1	MDDSTEREQ	SRL	TSCCLKREEMKL	Neutrokine alphaSV

	40	50	60	
17	LPKKTGGPQ	- - - - -	- - - - -	TNFalpha
8	F - - - -	- - - - -	- - - - -	TNFbeta
4	- - - -	- - - - -	- - - - -	LTbeta
30	LPCPTSVPR	RRPG	QRRPPPPPPPP	FasLigand
31	LPRKESPSV	RS	SKD - - -	Neutrokine alpha
31	LPRKESPSV	RS	SKD - - -	Neutrokine alphaSV

	70	80	90	
30	- - - - -	- - - - -	- - - - -	TNFalpha
9	- - - - -	- - - - -	- - - - -	TNFbeta
12	- - - - -	- - - - -	- - - - -	LTbeta
60	PPP - - -	- - - - -	- - - - -	FasLigand
58	SCCLTVVS	FF	YQVAA	Neutrokine alpha
58	SCCLTVVS	FF	YQVAA	Neutrokine alphaSV

FIG.2A

TNFalpha
TNFbeta
LTbeta
FasLigand
Neutrokinine alpha
Neutrokinine alphaSV

TNFalpha
TNFbeta
LTbeta
FasLigand
Neutrokin alpha
Neutrokin alphaSV

FIG. 2C

193	P	I	Y	L	G	G	V	F	Q	L	E	K	G	D	R	L	S	A	E	I	N	R	P	D	Y	L	D	F	A	E	TNFalpha
166	S	M	Y	H	G	A	A	F	Q	L	T	Q	G	D	Q	L	S	T	H	T	D	G	I	P	H	L	V	L	S	P	TNFBeta
204	S	V	G	F	G	L	V	Q	L	R	R	G	E	R	V	Y	V	N	I	S	H	P	D	M	V	D	F	A	R	LTbeta	
242	S	S	Y	L	G	A	V	F	N	L	T	S	A	D	H	L	T	V	N	V	S	E	L	S	L	V	N	F	E	E	FasLigand
244	S	C	Y	S	A	G	I	A	K	L	E	E	G	D	E	L	Q	L	A	I	P	R	E	N	A	Q	I	S	L	D	Neutrokin alpha
225	S	C	Y	S	A	G	I	A	K	L	E	E	G	D	E	L	Q	L	A	I	P	R	E	N	A	Q	I	S	L	D	Neutrokin alphaSV

223	S	G	Q	V	Y	F	G	I	I	A	L																					
196	S	-	T	V	F	F	G	A	F	A	L																					
234	-	G	K	T	F	F	G	A	V	M	V	G																				
272	S	-	Q	T	F	F	G	L	Y	K	L																					
274	G	D	V	T	F	F	G	A	L	K	L	L																				
255	G	D	V	T	F	F	G	A	L	K	L	L																				

FIG.2D

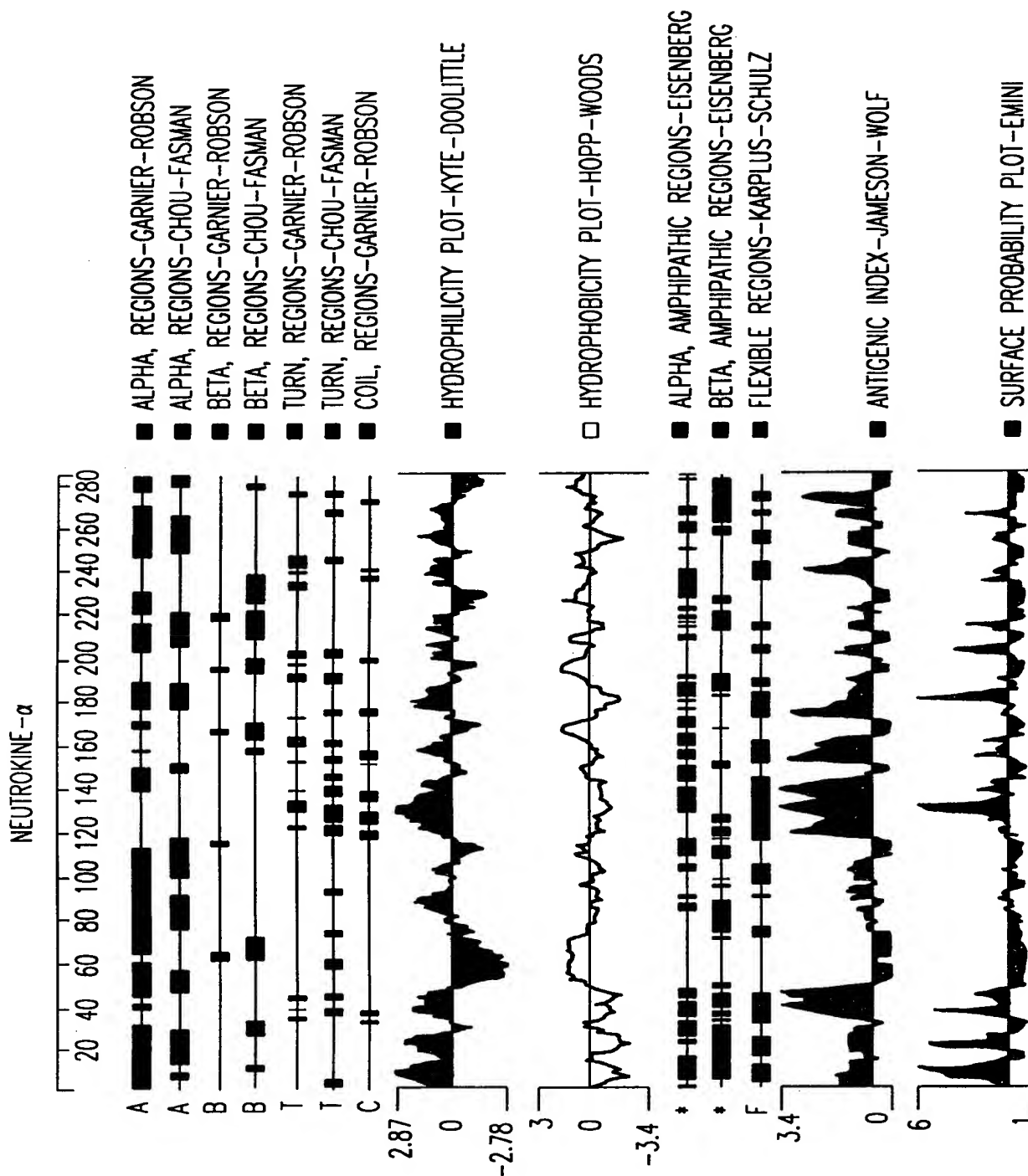


FIG.3

	1				50
HSOAD55RA	GGNTAACTCT	CCTGAGGGGT	GAGCCAAGCC	CTGCCATGTA
HNEDU15X	...AAATTCA	GGATAACTCT	CCTGAGGGGT	GAGCCAAGCC	CTGCCATGTA
HSLAH84R	.AATTCGGCA	NAGNAACTG	GTTACTTTT	TATATATGGT	CAGGTTTTAT
HLTBM08R	AATTCGGCAC	GAGCAAGGCC	GGCCTGGAGG	AAGCTCCAGC	TGTCACCGCG
	51				100
HSOAD55R	GTGCACGCAG	GACATCANCA	A..ACACANN	NNNCAGGAAA	TAATCCATTCT
HNEDU15X	GTGCACGCAG	GACATCAACA	A..ACACAGA	TAACAGGAAA	TGATCCATTCT
HSLAH84R	ATACTGATAA	GACCTACGCC	ATGGGACATC	TAGTTCAGAG	GAAGAAGGTC
HLTBM08R	GGACTGAAAA	TCTTTGAACC	ACCAGCTCCA	GGAGAAGGCA	ACTCCAGTCA
	101				150
HSOAD55R	CCTGTGGTCA	CTTATTCTAA	AGGCCCCAAC	CTTCAAAGTT	CAAGTAGTGA
HNEDU15X	CCTGTGGTCA	CTTATTCTAA	AGGCCCCAAC	CTTCAAAGTT	CAAGTAGTGA
HSLAH84R	CATGTCTTTG	GGGATGAATT	GAGTCTGGTG	ACTTTGTTTC	GATGTATTCA
HLTBM08R	GAACAGCAGA	AATAAGCGTG	CCGTTTCAGG	TCCAGAAGAA	ACAGTCACTC
	151				200
HSOAD55R	TATGGATGAC	TCCACAGAAA	GGGAGCAGTC	ACGCCTTACT	TCTTGCCTTA
HNEDU15X	TATGGATGAC	TCCACAGAAA	GGGAGCAGTC	ACGCCTTACT	TCTTGCCTTA
HSLAH84R	AAATATGCCT	GAAACACTAC	CCAATAATTC	CTGCTATTCA	GCTGGCATTG
HLTBM08R	AAGACTGCTT	GCAACTGNNT	GCAGACAGTG	AAACACCAAC	TATACAAAAA
	201				250
HSOAD55R	AGAAAAGAGA	AGAAATGAAA	CTGNAAGGAG	TGTGTTTCCA	TCCTCCCACG
HNEDU15X	AGAAAAGAGA	AGAAATGAAA	CT.GAAGGAG	TGTGTTTCCA	TCCTCCCACG
HSLAH84R	CAAACTGGN	AGGAAGGA..	...GATGAAC	TCCAACCTGC	AATACCAGGG
HLTBM08R	GGCTCCCTTC	TGNTGCCACA	TTTGGGCCAA	GGAATGGAGA	GATTTCTTCG
	251				300
HSOAD55R	GAAGGAAAGC	CCCTCTNTCC	GATCCTCCAA	AGACGGAAAG	CTGCTGGCTG
HNEDU15X	GAAGGAAAGC	CCCTCTGTCC	GATCCTCCAA	AGACGGAAAG	CTGCTGGCTG
HSLAH84R	GAAAATGCAC	AATTATCACT	GGGATGGAGA	TGTTACACATT	TTTTGGGTGC
HLTBM08R	TCTGGAAACA	TTTTGCCAAA	CTCTTCAGAT	ACTCTTNCT	CTCTGGGAAT
	301				350
HSOAD55R	CAACCTTGNT	GNTGGCATTG	TGTTCTTGCT	GNCTCAAGGT	GGTGTTNTT.
HNEDU15X	CAACCTTGCT	GCTGGCACTG	CTGTCTTGCT	GCCTCACGGT	GGTGCTTTTC
HSLAH84R	CATTGAAACT	GCTGTGACCT	NCTTACANCA	NGTGCTGTTN	GCTATTTTNC
HLTBM08R	CAAAGGAAAA	TCTCTACTTA	GATTNACACA	TTTGTTCCCA	TGGGTNTCTT
	351				400
HSOAD55R
HNEDU15X	TACCAGGTGG	CCGCCCTGCA	AGGGGACCTG	GCCAGCCTCC	GGGCAGAGCT
HSLAH84R	CTNCCTNTTC	TNTGGTAACC	TCTTAGGAAG	GAAGGATTCT	TAAGTGGGAA
HLTBM08R	AAGTTTTAAA	AGGGGAGTGC	CCTTAGGAGG	AAAAGGGGAT	AAATATTGGC

FIG.4A

15

SUBCLASS

	102	103	104	105	106
HSOAD55R
HNEDU15X	GCAGGGCCAC	CACGCGGAGA	AGCTGCCAGC	AGGAGCAGGA	GCCCCCAAGG
HSLAH84R	ATAACCCAAA	AAAANNTTAA	ANGGGTANGN	GNNANANGNG	GGGNNGTTNN
HLTBM08R	CAAGGNACTG	GTTANTTTNT	AAATATGGTC	AGGTTTNTAT	ANCTGGTAGG

	451				500
HS0AD55R
HNEDU15X	CCGGCCTGGA	GGAAGCTCCA	GCTGTCACCG	CGGGACTGAA	AATCTTTGAA
HSLAH84R	CNNGNNGNNT	TTTNGGNNTA	TNTTNTNNTN	GGGNNGNGTA	AAAATGGGGC
HLTBM08R	CCTCGCCATG	GGCATTNATT	CANGGNGAGG	NCNNTCTTTT	GGGNTGA...

	501				550
HSOAD55R
HNEDU15X	CCACCAGCTC	CAGGAGAAGG	CAACTCCAGT	CAGAACAGCA	GAAATAAGCG
HSLAH84R	CNANGGGGGN	TTTTT.....
HLTBM08R

	551					600
HSOAD55R					
HNEDU15X	TGCCGTT	CAG	GGTCCAGAAG	AAACAGTCAC	TCAAGACTGC	TTGCAACTGA
HSLAH84R					
HLTBM08R					

601 650

HSOAD55R
HNEDU15X TTGCAGACAG TGAAACACCA ACTATACAAA AAGGATCTTA CACATTTGTT
HSLAH84R
HI TBM08R

	651		700
HSOAD55R
HNEDU15X	CCATGGCTTC	TCAGCTTTAA	AAGGGGAAGT GCCCTAGAAG AAAAAGAGAA
HSLAH84R
HI TBM08R

701 750

HSOAD55R
HNEDU15X
HSLAH84R
HITBM08R

.....
TAAAATATTG GTCAAAGAAA CTGGTTACTT TTTTATATAT GGTCAGGTTT
.....
.....

751 800

HSOAD55R
HNEDU15X TATATACTGA TAAGACCTAC GCCATGGGAC ATCTAATTCA GAGGAAGAAG
HSLAH84R
HI TRM08R

FIG. 4B

APPROVAL	FIG.	
DRAFTSMAN	CLASS	SUBCLASS

	801		850
HSOAD55R
HNEDU15X	GTCCATGTCT	TTGGGGATGA	ATTGAGTCTG GTGACTTTGT TTCGATGTAT
HSLAH84R
HLTBM08R
	851		900
HSOAD55R
HNEDU15X	TCAAAATATG	CCTGAAACAC	TACCCAATAA TTCCTGCTAT TCAGCTGGCA
HSLAH84R
HLTBM08R
	901		950
HSOAD55R
HNEDU15X	TTGCAAACT	GGAAGAAGGA	GATGAACTCC AACTTGCAAT ACCAAGAGAA
HSLAH84R
HLTBM08R
	951		1000
HSOAD55R
HNEDU15X	AATGCACAAA	TATCACTGGA	TGGAGATGTC ACATTTTTTG GTGCATTGAA
HSLAH84R
HLTBM08R
	1001		1050
HSOAD55R
HNEDU15X	ACTGCTGTGA	CCTACTTACA	CCATGTCTGT AGCTATTTTC CTCCCTTTCT
HSLAH84R
HLTBM08R
	1051		1100
HSOAD55R
HNEDU15X	CTGTACCTCT	AAGAAGAAAG	AATCTAACTG AAAATACCAA AAAAAAAAAA
HSLAH84R
HLTBM08R
	1101		
HSOAD55R		
HNEDU15X	AAAAAA		
HSLAH84R		
HLTBM08R		

FIG.4C

APPRO	FIG.	
DES	SUBCLASS	
DRAFTSMAN		

Neutrokin- α SV

1	ATGGATGACTCCACAGAAAGGGAGCAGTCACGCCTTACTTCTTGCCTTAAGAAAAGAGAA	60
1	M D D S T E R E Q S R L T S C L K K R E	20
61	GAAATGAAACTGAAGGAGTGTGTTTCCATCCTCCACGGAAGGAAAGCCCCTCTGTCCGA	120
21	E M K L K E C V S I <u>L P R K E S P S V R</u>	40
CD-I		
121	TCCTCAAAGACGGAAAGCTGCTGGCTGCAACCTTGCTGCTGGCACTGCTGTCTTGCTGC	180
41	<u>S S K D G K L L A A T L L L A L L S C C</u>	60
CD-I		
181	CTCACGGTGGTGTCTTTCTACCAGGTGGCCGCCCTGCAAGGGGACCTGGCCAGCCTCCGG	240
61	<u>L T V V S F Y Q V A A L Q G D L A S L R</u>	80
CD-II		
241	GCAGAGCTGCAGGGCCACCACGCGGAGAAGCTGCCAGCAGGAGCAGGAGCCCCAAGGCC	300
81	<u>A E L Q G H H A E K L P A G A G A P K A</u>	100
CD-II CD-III		
301	GGCCTGGAGGAAGCTCCAGCTGTCACCGCGGGACTGAAAATCTTTGAACCACCAGCTCCA	360
101	<u>G L E E A P A V T A G L K I F E P P A P</u>	120
CD-III		
#		
361	GGAGAAGGCAACTCCAGTCAGAACAGCAGAAATAAGCGTGCCGTTCAAGGTCCAGAAGAA	420
121	G E G N S S Q N S R N K R A V Q G P E E	140
421	ACAGGATCTTACACATTTGTTCCATGGCTTCTCAGCTTTAAAAGGGGAAGTGCCCTAGAA	480
141	T G S Y T F <u>V P W L L S F K R G S A L E</u>	160
CD-IV		
481	GAAAAAGAGAATAAAATATTGGTCAAAGAACTGGTTACTTTTTATATATGGTCAGGTT	540
161	<u>E K E N K I L V K E T G Y F F I Y G Q V</u>	180
CD-IV CD-V		
541	TTATATACTGATAAGACCTACGCCATGGGACATCTAATTCAGAGGAAGAAGGTCCATGTC	600
181	<u>L Y T D K T Y A M G H L I Q R K K V H V</u>	200
CD-VI CD-VII		

FIG.5A

APPROV.	FIG. 5B	
5	CLASS	SUBCLASS
DRAFTSMAN		

Neutrokin- α SV

```

601 TTTGGGGATGAATTGAGTCTGGTGACTTTGTTTCGATGTATTCAAAATATGCCTGAAACA 660
201 F G D E L S L V T L F R C I Q N M P E T 220
      CD-VIII                      CD-VIII

661 CTACCCAATAATTCCTGCTATTTCAGCTGGCATTGCAAACTGGAAGAAGGAGATGAACTC 720
221 L P N N S C Y S A G I A K L E E G D E L 240
      CD-IX                      CD-X

721 CAACTTGCAATACCAAGAGAAAATGCACAAATATCACTGGATGGAGATGTCACATTTTTT 780
241 Q L A I P R E N A Q I S L D G D V T F F 260
      CD-X                      CD-XI

781 GGTGCATTGAAACTGCTGTGACCTACTTACACCATGTCTGTAGCTATTTTCCTCCCTTTC 840
261 G A L K L L 266
      CD-XI

841 TCTGTACCTCTAAGAAGAAAGAATCTAACTGAAAATACCAAAAAAAAAAAAAAAAAAAAA 900

901 AAA 903

```

FIG.5B

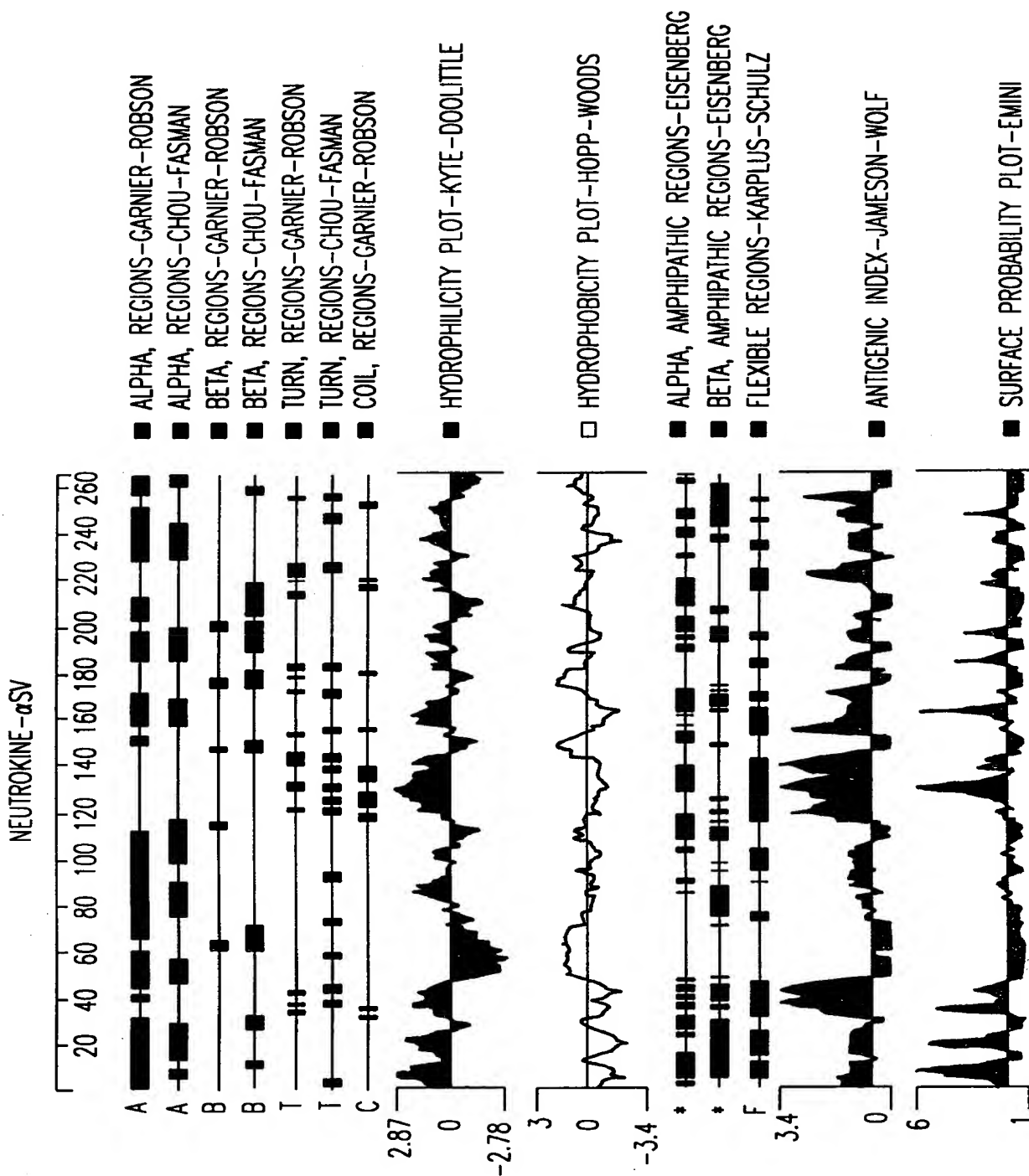


FIG.6

Neutrokinine-

Alpha MDDSTEREQSRLTSCCLKREEMKLKECVSILPRKESPSVRS 41

Transmembrane Region

SKDGKLLAATLLALLSCCLTVVSFYQVAALQGDLASLRAE 82

LQGHHAELPAGAGAPKAGLEEAPAVTAGLKIFEPPAPGEG 123

NSSQNSRNKRAVQGPEETVTQDCLQLIADSEPTIQKGSYT 164
 Apr11 HSLHLVPIINATSK-DDSDVT 134
 TNF KPVAVHVVANPQAEQG----- 102
 LTα KPAAHLIGDPSKQNS----- 76

FV P W L L S - - - - F K R G S A L E E K E N K I L V K E T G Y F F I Y G Q V L 200 EV M W Q P A - - - - L R R G R G L Q A Q G Y G V R I Q D A G V Y L L Y S Q V L 170 - L Q W L N R R A N A L L A N G V E L R D - - N Q L V V P S E G L Y L I Y S Q V L 139 - L L W R A N T D R A F L Q D G F S L S N - - N S L L V P T S G I Y F V Y S Q V V 114	A' B' B C
Y T D K T Y - - - - A M G H L I Q R K K V H V F G D E L S L V T L F R C I Q N M P 237 F Q D V I F - - - - I M G Q V V S R E - - - - G Q G R Q E T L F R C I R S M P 201 F K G Q G C P - - - - S T H V L L T H I S R I A V S Y Q T K V N L L S A I K S P 176 F S G K A Y S P K A I S S P L Y L A H E V Q L F S S Q Y P F H V P L L S S Q K M V 155	D E

FIG.7A-1

APPROVED	G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

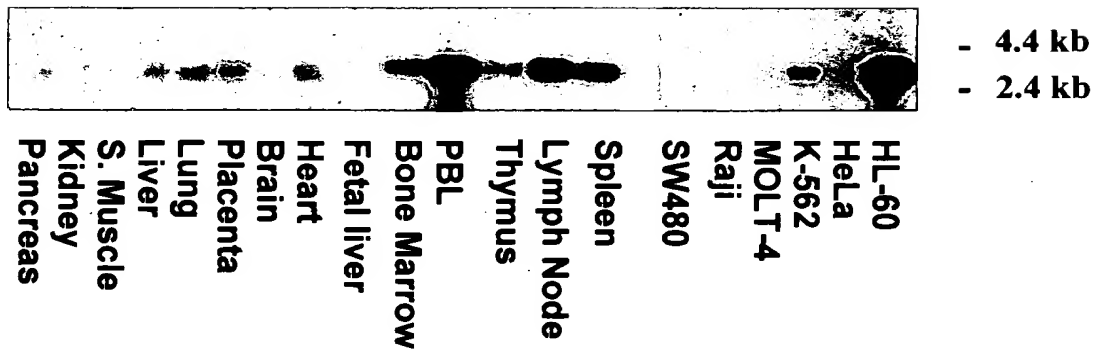


FIG.7B

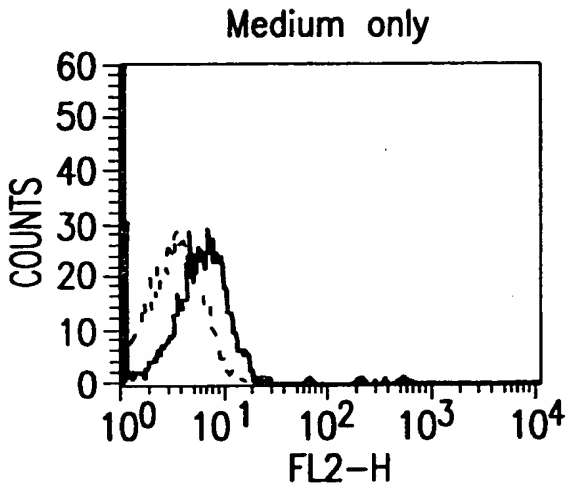


FIG.8A

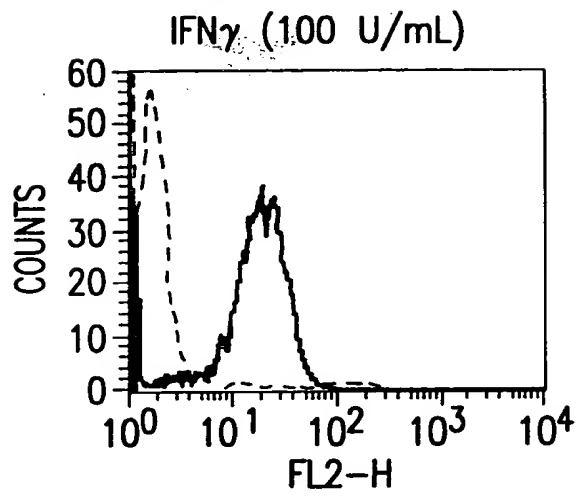


FIG.8B

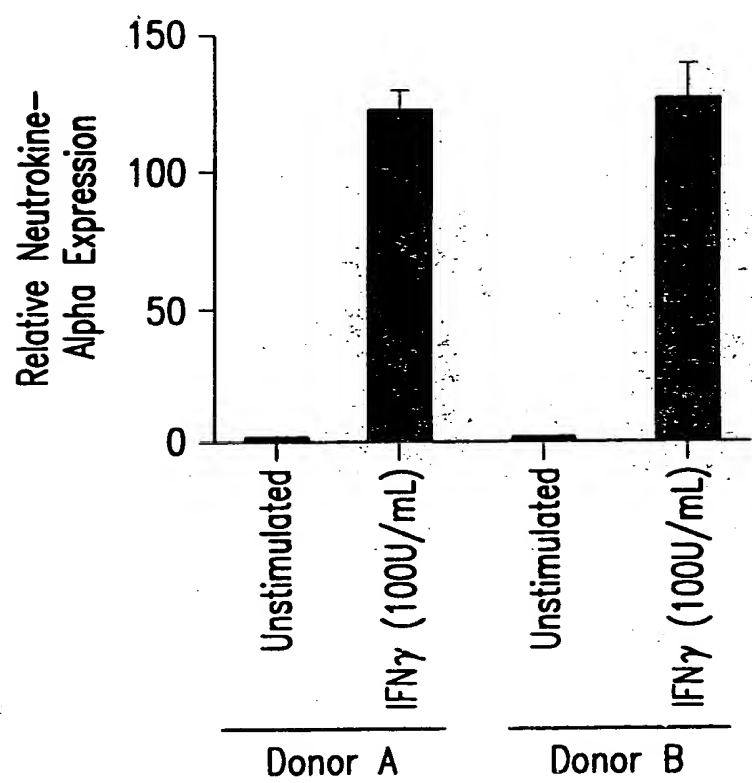


FIG.8C

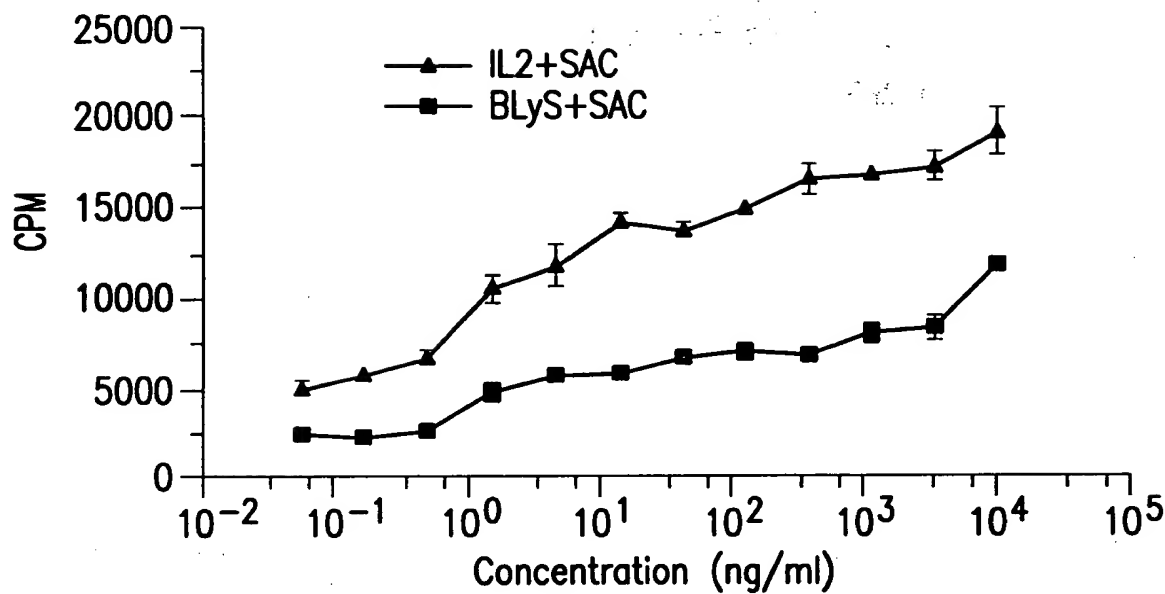


FIG. 9A

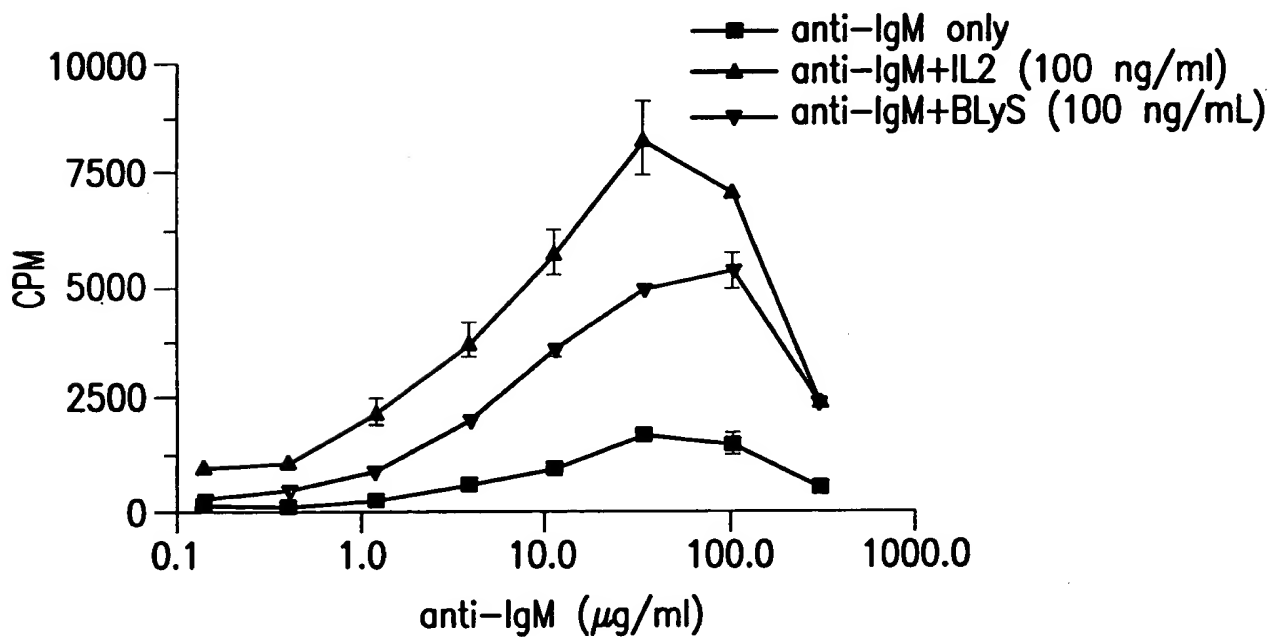


FIG. 9B

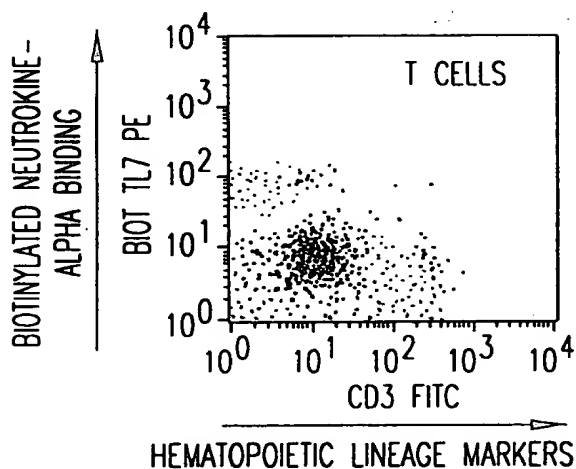


FIG.10A

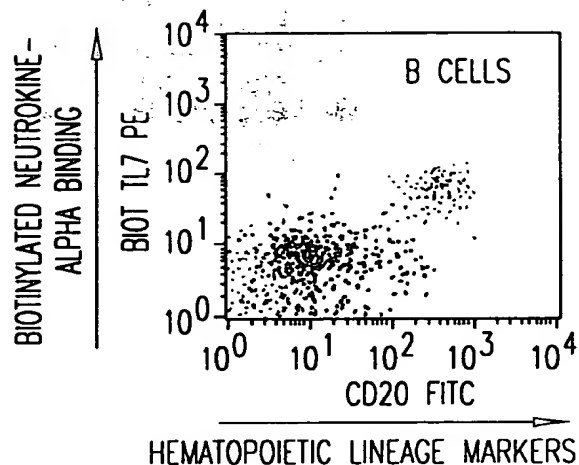


FIG.10B

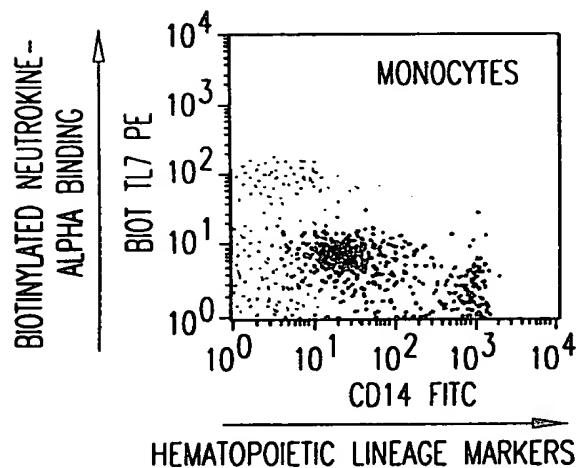


FIG.10C

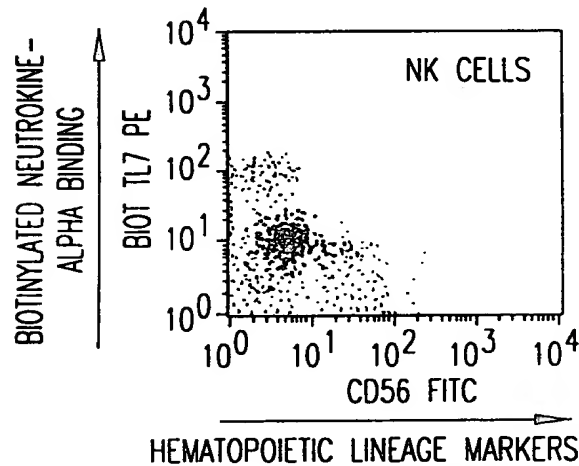


FIG.10D

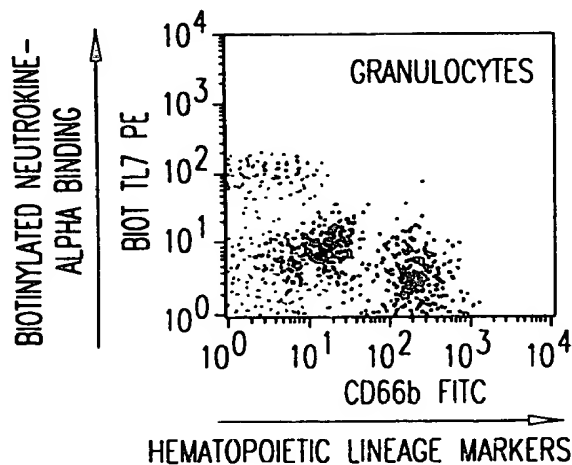


FIG.10E

APP	FIG.	
	CLASS	SUBCLASS
DRAFTSMAN		

U-937

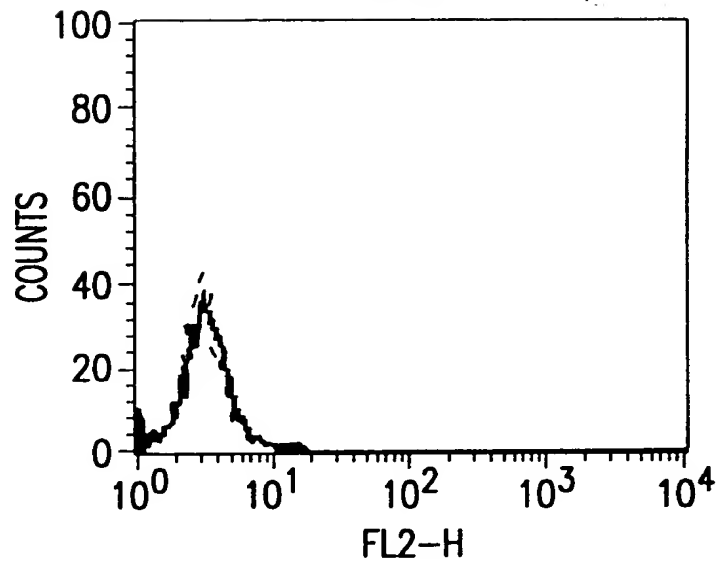


FIG.10F

IM-9

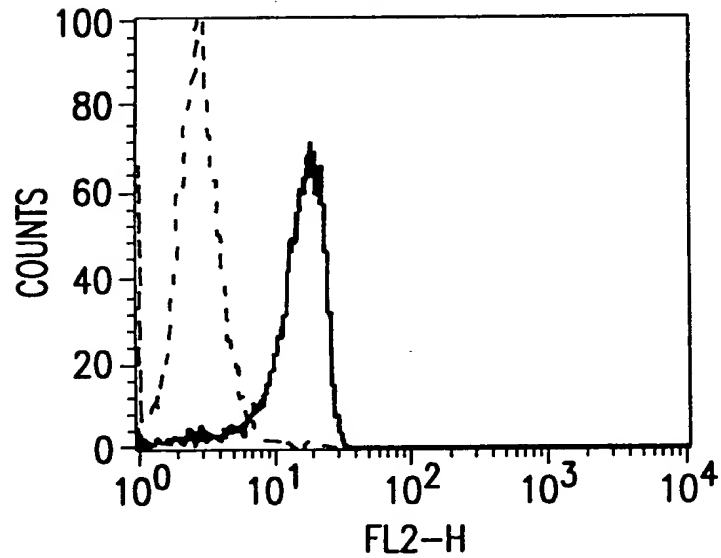
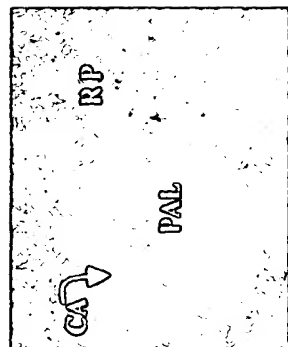


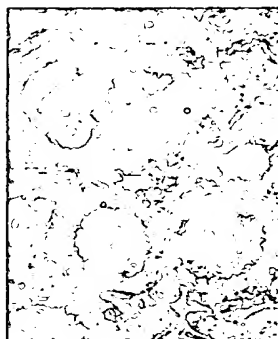
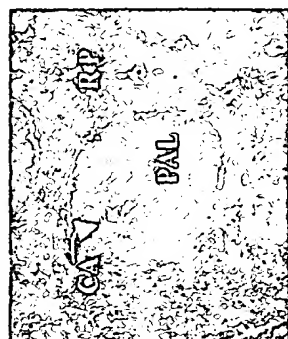
FIG.10G

APPROVED	O.G. FIG.	
BY	CLASS	SUBCLASS
DRAFTSMAN		

Neutrokine - alpha
treated spleen
(2mg/Kg) bid 4d



Normal spleen



H & E (100X)

CD45R(B220)
(40X)

FIG.11A

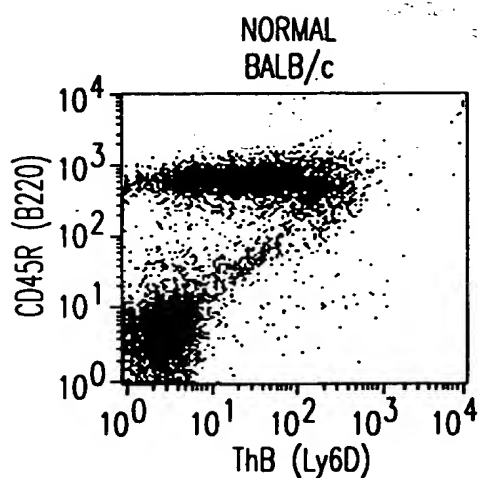


FIG. 11B

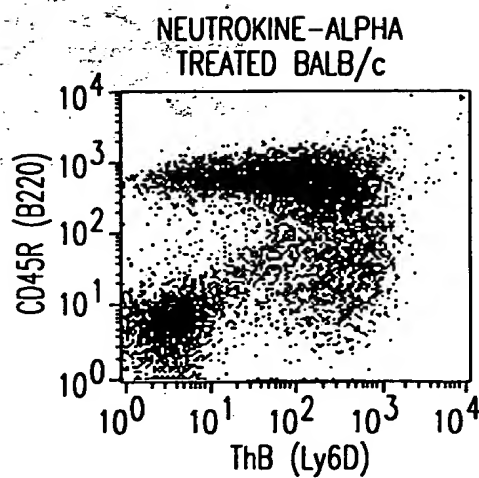


FIG. 11C

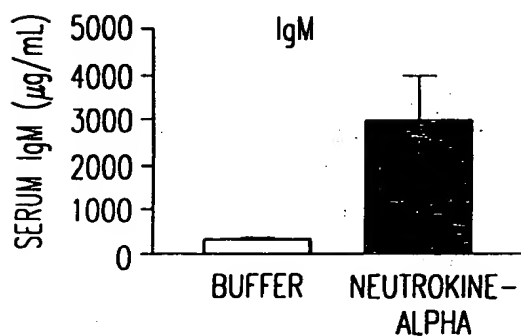


FIG. 11D

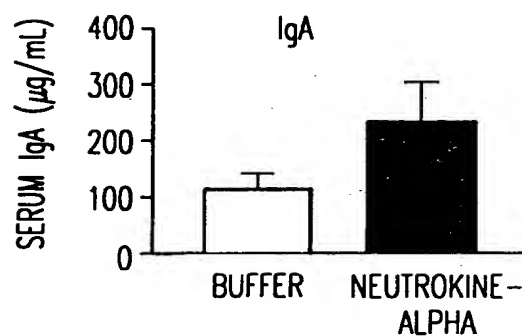


FIG. 11E

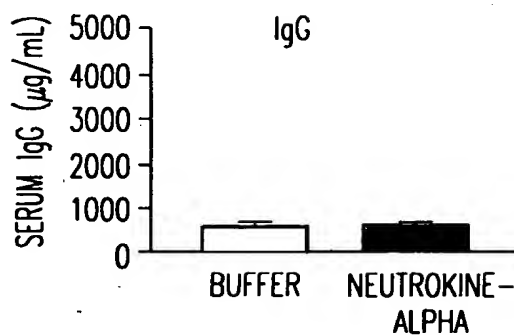


FIG. 11F